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Date of Signature and Deposit: 4/18/03

Jean C. Baker, Reg. No. 35,433

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.: 09/530,233
Applicants: Philippe Seguela, et al.
Filed: April 26, 2000
Title: DNA ENCODING A HUMAN PROTON-GATED ION CHANNEL AND USES THEREOF
TC/A.U.: 1646
Examiner: M. Pak
Docket No.: 641050.90021

Honorable Commissioner for Patents
Washington, DC 20231

DECLARATION OF PHILIPPE SEGUELA AND KAZIMIERZ BABINSKI

We, Philippe Seguela and Kazimierz Babinski, declare that:

1. We are the named inventors of the above-identified patent application. Kazimierz Babinski is a pharmacist by training (B. Pharm.) with post-graduate studies in pharmaceutical science/pharmacology. He is now a Ph.D. student and President/General Director of Antalium, Inc. (Montreal, Quebec) a company concerned with commercializing technology involving the above-identified patent application. Philippe Seguela is an Associate Professor in the Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada. His area of expertise is the molecular biology of ligand-gated ion channels with a particular focus on ATP-gated

ion channels (P2X family) and proton-gated ion channels (ASIC family).

2. We have been asked to review the outstanding Office Action in the above-identified patent application and comment on the Examiner's rejection of claims 16 - 21 as being anticipated by Waldman (J. Biol. Chem., 1997) and all claims as being anticipated by Lewis, et al. (Nature, 1995). We assert that neither disclosure anticipates our invention.

3. The Examiner has rejected pending claims 16-21 as being anticipated by Waldman (J. Biol. Chem., 1997). This reference describes the cloning in COS cells of a novel proton-gated Na^+ channel subunit expressed in Dorsal Root Ganglia (DRG) and identified as DRASIC (Rat Dorsal Root Ganglion Acid Sensitive Ion Channel). While there are apparent similarities between DRASIC and the proton-gated ion channel that is the subject of the present application, it should be noted that there are fundamental differences between them as well. As indicated at page 3 of the specification, hASIC3 is not the ortholog of rat DRASIC, and evidence for this is presented below this statement. Based on this information, we assert that what we have discovered is a novel proton-gated ion channel that has no counterpart in other species. Consequently, it is respectfully submitted that the Waldman reference does not anticipate the present invention.

4. The Examiner has rejected all pending claims as being anticipated by Lewis, et al. (Nature, 1995). As was the

case with the Waldman reference (discussed above), the Lewis reference relates to the identification and characterization of a novel heteropolymeric P2X channel comprised of $P2X_2$ and $P2X_3$ subunits and present in rat dorsal root ganglia (DRG). The ion channel subunits described in the Lewis reference, namely rat $P2X_2$ and rat $P2X_3$, and that which is the subject of the present application belong to two distinct gene families and have an amino acid sequence identity of less than 25% when aligned with the amino acid sequence of SEQ ID No. 2 of the present application (see attached alignment results). We assert that the sequences are not orthologs and fervently believe that our newly-discovered ion channel is unlike those previously known in the art. Furthermore, the present application describes a heteropolymeric ion channel resulting from the interaction of ion channel subunits belonging to two distinct gene families, namely ASIC3 (Proton-gated ion channel family) and $P2X_2$ (ATP-gated ion channel family). In contrast, the Lewis, et al. reference describes a heteropolymeric ion channel comprised of ion channel subunits belonging to the same gene family, namely $P2X_2$ and $P2X_3$ (ATP-gated ion channel family).

5. We declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like made are punishable by

fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

Respectfully submitted,

Dated: 04/17/03

P. Seguela

Philippe Seguela

Dated: April 17, 2003

Kazimierz Babinski

Kazimierz Babinski